Physiotherapy in Cystic Fibrosis: a comprehensive clinical overview

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Abstract

Physiotherapy remains the cornerstone of cystic fibrosis (CF) management alongside medical treatment. Traditionally, physiotherapy intervention focussed on airway clearance during the clinically stable stage and chest infections. Research evidence consistently supports greater mucus clearance with chest physiotherapy compared to cough alone or no treatment. Various methods and techniques of airway clearance have been developed and investigated, and data suggest that most of them are of similar effectiveness. Nowadays physiotherapy management also extends to other areas, supported by studies and clinical practice. The physiotherapists plan, supervise and follow-up systematic exercise or personalised rehabilitation programs, which, similarly to airway clearance, are recommended in all patients with CF. Furthermore, based on a comprehensive assessment, physiotherapists incorporate the management of accompanying musculoskeletal problems such as back pain and postural disorders, as well as urine incontinence issues. In the era that aims to improve quality of life, it is essential that physiotherapists are aware of specific conditions that might affect the management of CF. Their role is to work alongside and within the CF multi-disciplinary team throughout patient's treatment and consistently support the patient and carers, in particular whilst on clinical pathways of the lung transplantation and palliative care.

Keywords: physiotherapy, cystic fibrosis, airway clearance, exercise

INTRODUCTION

Cystic Fibrosis (CF) is a recessive genetic disease that affects the patient on multiple systems, with profound manifestations in the respiratory and digestive systems [1]. It is characterised by the mutation and therefore dysfunction of the gene for the cystic fibrosis transmembrane conductance regulator (CFTR). This protein mainly functions as an ion channel, regulating fluid volume on epithelial surfaces via chlorine secretion and inhibition of sodium resorption. In the airways of the patients with CF, dysfunction of the CFTR results in periciliary liquid layer depletion [2]. Clinically, patients with CF present abnormal consistency and high volumes of sputum, cough, dyspnoea, bronchiectasis and weight loss. As the survival of these patients is increasing, it is crucial that health care professionals address symptoms and support individuals in evolving issues developed throughout their life span.

Physiotherapy is an integral part of the therapeutic management of CF patients, both at the clinically stable stage of the disease and during respiratory infections. In the past, physiotherapy was focused on airway clearance, also known as chest physiotherapy, by teaching or applying methods such as the postural drainage with or without the additional application of manual techniques [3]. Postural drainage of the tracheobronchial tree uses specific gravitational positions to assist mucus mobilisation downwards (towards the mouth) within the airways. Manual techniques (percussions, vibrations and/or shakes) use mechanical forces to assist the detachment of mucus from the airway epithelium and its mobilisation. Nowadays, the choice of airway clearance techniques has been expanded to newer methods such as the autogenic drainage, the active cycle of breathing techniques (ACBT), the use of positive expiratory pressure (PEP) devices with or without oscillation, and others. Still, modern physiotherapy in CF also includes the assessment of the cardiovascular system and improvement of the patient's fitness level, muscle strength and endurance through exercise, as well as specialised interventions to improve musculoskeletal symptoms of pain, posture and incontinence [4].

PHYSIOTHERAPY

Airway clearance

Patient education, application and monitoring of the airway clearance techniques remains the main physiotherapy treatment for patients with CF [4]. Physiotherapists facilitate the establishment of an individualised airway clearance routine by supporting patients and their families to establish regular regimes during a clinically stable stage and have an escalation plan for disease exacerbations [5]. Airway clearance is usually performed on a daily basis and as required. The selected method applied, duration and frequency of each session are tailored to the patient, their general health condition and the severity of the disease. For instance, airway clearance becomes more regular during exacerbations or hospitalisations [6]. Hospitalisations also provide an opportunity for physiotherapists to re-assess the effectiveness of daily airway clearance and provide appropriate feedback and guidance for improving the patient's usual technique prior to discharge.

Table 1 presents the main categories of airway clearance techniques and methods in CF. Those can be used in isolation or in combination regimes. The effectiveness of airway clearance is extensively supported in the literature, when compared to no airway clearance or cough alone [4, 7-9]. A recent systematic review supported a significant increase in the amount of sputum (wet or dry) in the patient groups that applied airway clearance using postural drainage with or without the addition of manual techniques or using PEP, compared to spontaneous cough or not using any technique [7]. The weight of the sputum was higher after the application of the active cycle of breathing techniques compared to the use of the flutter (an oscillating PEP device) or high frequency chest wall oscillation (vest) [10]. The weight of the sputum expectorated was greater after using the PEP mask compared to autogenic drainage, postural drainage positions and their combination, although this difference is short-term (up to one week) [11]. On the other hand, there is no difference in the amount of the

expectorated mucus after autogenic drainage compared to the flutter, or between the high frequency chest wall oscillation compared to the autogenic drainage or the PEP mask for longer time-intervals [10, 12].

Systematic reviews did not show significant differences in the lung function (FEV_1) of adult patients following the use of PEP, when assessed patients prior and immediately after a physiotherapy session or up to 3 months later [7, 10, 11, 13]. Additionally, the lung function did not change after applying the active cycle of breathing techniques in combination with the PEP mask, postural drainage with or without manual techniques, or the high frequency chest wall oscillation [12]. However, treatment in children and adolescents that was applied up to one year showed 6% increase in FEV_1 with the use of PEP [13].

Regarding the hospitalisation frequency, no differences were found for those who practiced the active cycle of breathing techniques compared to the postural drainage with or without manual techniques [12]. The number of hospitalisations, however, was lower for those who used PEP than the patients who used the flutter (5 vs 18 hospitalisations, respectively) [10]. Similarly, fewer patients used intravenous antibiotics from the group that used PEP devices, compared to the group of the high frequency chest wall oscillation [13].

For the quality of life, there is no difference amongst techniques and devices, such as the postural drainage with or without manual techniques, active cycle of breathing techniques, autogenic drainage, PEP mask, flutter, and cornet [10, 12, 13]. However, patients preferred the PEP mask for long-term use (>1 month), and also preferred seating instead of using postural drainage positions [10, 11, 13]. Autogenic drainage was preferred among children between 12-18 years old, compared to postural drainage in combination with manual techniques [14].

Important factors for the success of the selected airway clearance plan is the compliance to treatment and patient satisfaction. Factors that increase the rate of compliance is good patient knowledge of the technique and confidence in its application, independence and preference [15, 16]. Evidence indicate that patient who receive help, those who produce more sputum, and children with CF whose parents believe in the necessity of treatment are those with higher compliance in airway clearance [17, 18].

Airway clearance adaptations

Mucolitics and other agents

Patients with CF often receive medications that aim to increase the effectiveness of airway clearance, such as nebulised hypertonic saline (3% to 7% NaCl), dornase alpha (DNase), and mannitol. The use of inhaled hypertonic saline (osmotic pressure > 0.9% NaCl) in patients with CF is considered to improve the rheological characteristics of sputum and increase the hydration of the airway epithelium; thus, increase the sputum motility and facilitate the mucus clearance [19]. There is good evidence that the use of hypertonic saline reduces the incidence of respiratory infections, improves the quality of life, and increases FEV_1, although the changes are not maintained in the long term (48 weeks) [20, 21]. During the hospitalisation of patients with CF, hypertonic saline improves the chances of quick return of the lung function (FEV_1) to pre-infectious levels [22]. With regards to timing the hypertonic saline administration, a recent systematic review supports its use before or during the performance of airway clearance, rather than its administration afterwards [23]. If the prescribed doses are two, it is recommended to administer one the morning and one in the evening, and if the patient receives a single dose this is given at a convenient time chosen by the patient [23].

Dornase alpha (DNase) is a recombinant human deoxyribonuclease that reduces sputum viscosity by selectively hydrolysing the large extracellular DNA molecules contained in the mucus into smaller structures, thereby increasing the potential for its elimination [24]. This drug is administered via a jet-nebuliser device and has been shown to increase respiratory function, improve quality of life, and reduce the incidence of respiratory infections [24]. With regards to timing its administration, it appears that using DNase before or after airway clearance does not have any difference in improving lung function (FEV_1 and FVC) or patient's quality of life [25, 26]. In clinical practice, physiotherapy often follows the proposed guidelines of the pharmaceutical company to perform airway clearance 30 minutes after the DNase administration [27].

Inhaled mannitol is a naturally occurring sugar alcohol which enhances osmosis, causing mucus hydration [28]. Inhaled mannitol is administered as dry powder (capsules) using an inhaler. As demonstrated by two 26-week multi-centre studies with a total number of 600 participants with CF, inhaled mannitol improves the respiratory function of patients but does not improve their quality of life [29, 30]. Although its use usually precedes airway clearance in clinical practice, there is no research data to compare different timings of administration.

Haemoptysis

Haemoptysis is a major change in the patient's clinical presentation and may be life-threatening. The physiotherapy assessment should include questions about sputum description and reference to current or past haemoptysis episodes. Active frank haemoptysis (>100-1000 ml haemoptysis in 24 hours or 48 hours) is treated exclusively medically, e.g. with bronchial embolisation of the arteries or thoracic surgery, while the airway clearance treatment is temporarily discontinued [31, 32]. In moderate or low haemoptysis, physiotherapists, in collaboration with the medical team, decide whether or not it is appropriate to continue airway clearance using clinically reasoning. If the

treatment is appropriate and safe to continue, then the active cycle of breathing techniques or autogenic drainage is often selected over other techniques.

Pneumothorax

Spontaneous pneumothorax is a common complication in patients with CF. It is associated with a reduction in pulmonary function and 50-90% chance of recurrence [32, 33]. If the pneumothorax occurs for the first time and it is small, then it can be treated conservatively with oxygen supply [34]. In patients continuing airway clearance, it is suggested to liaise with the medical team for adding humidification to the oxygen supply and ensuring adequate analgesia for the duration of the treatment sessions [35]. In the case of large pneumothorax (> 2 cm between parietal pleura and visceral pleura) or recurrent pneumothorax, chest drainage is performed using thoracic catheters, while in resistant cases patients might get pleurodesis [34]. Positive pressure devices such as PEP, flutter and acapella are contraindicated in the presence of pneumothorax [34]. Regarding physical activity, patients need to be engaged with moderate activities but should avoid bearing weights over 2 kg or strenuous aerobic exercise for a period of two to six weeks after the complete drainage of the pneumothorax [34].

Exercise

Exercise is an integral part of the comprehensive physiotherapy intervention for patients with CF [36]. American College of Sports Medicine guidelines advocate 3-5 sessions of moderate exercise per week, with the aim to adopt exercise as a way of living [37]. Benefits of specific exercise modalities in cystic fibrosis are yet to be identified in methodologically strong studies [38]. Despite research interest, evidence has not established the effectiveness of inspiratory muscle training on this group of patients, therefore this is currently not routinely incorporated in the CF treatment. In the clinical setting, the assessment of patients with CF uses simple and cost-effective exercise field

tests, such as the 6-minute walk test (6MWT) and the incremental shuttle walk test (ISWT), whilst the level of dyspnoea is assessed using the Borg dyspnoea scale [39].

Exercise can theoretically assist airway clearance through the kinetic forces and vibrations generated within the airways, but it cannot substitute for the formal airway clearance [40]. When compared to airway clearance techniques, moderate aerobic exercise leads to less mucus expectoration [41]. Also, exercise as a single agent does not increase cough immediately after its completion, although it improves the subjective ease of sputum clearance [42]. Clinically, exercise is mainly used additionally to airway clearance, as a means to improve the exercise capacity of the patient and is usually performed before the implementation of airway clearance.

Exercise considerations

Musculoskeletal and postural issues

Back and thoracic pain are frequently reported in patients with CF, although they do not have an effect on lung function [43, 44]. Higher thoracic kyphosis is associated with lower lung function, but compared to a few years ago it is nowadays more uncommon [45]. Low bone density and osteopenia is also a common issue in patients with CF **[46, 47]**. Counselling and appropriate exercise programs from physiotherapists can potentially address and improve these postural and structural issues [36].

Urinary incontinence

Surveys show that urinary incontinence in patients with CF is reported in 30% to 68% of women or girls and 5% to 16% of men or boys [48-51]. The dynamic pressure created during coughing is potentially a key mechanism of CF urinary incontinence, although it may not be the only one [52].

Coughing, sneezing, laughing and spirometry are among the activities that trigger urinary incontinence incidents [53]. Incontinence worsens during respiratory infections and has been associated with poorer quality of life and higher anxiety and depression scores [51, 54, 55]. Assessing incontinence using screening tools and clarifying questions should be an integral part of the CF physiotherapy assessment, regardless of gender [56]. Physiotherapy treatment of urinary incontinence includes counselling and specialised training involving pelvic floor exercises, such as Kegel exercises [55, 57, 58].

Diabetes mellitus

Diabetes mellitus is associated with CF and is the most common comorbidity of the disease, occurring in up to 20-50% of adult patients [59-61]. This comorbidity requires the co-operation of the physiotherapists with the endocrine team, especially for the patients who require insulin therapy [62]. Additionally, the presence of diabetes mellitus needs to be considered in the physiotherapy plan, mainly in the exercise prescription and performance. In this case, the proper scheduling of the meal times or insulin intake is essential.

Quality of life

Over time and as the CF severity and symptoms progress, the quality of life of patients is deteriorating. Females with CF often report poorer quality of life compared to their male age-matched peers [63]. Although the correlation between lung function and quality of life is weak to moderate, patients with better lung function report higher quality of life [54]. Also, the presence of *Pseudomonas aeruginosa* and frequent respiratory infections appear to have a negative impact on the quality of life of patients [54].

Researchers use a number of validated questionnaires for the assessment of quality of life of people with CF, and clinician physiotherapists can use the same tools for their patients. Those include: generic questionnaires or questionnaires for a specific disease symptom, such as the Short Form-36 (SF-36) and the Leicester Cough Questionnaire, respectively [64, 65]; disease-specific questionnaires, such as the Manchester Questionnaire, the Cystic Fibrosis Questionnaire-Revised and the Cystic Fibrosis-Quality of Life [64, 66-69]; and questionnaires for babies and children of young age, such as the Modified Parent Cystic Fibrosis Questionnaire-Revised [70].

Special considerations

Long term oxygen therapy and non-invasive ventilation

A recent systematic review in patient with CF did not show long-term benefits from the long-term oxygen therapy, in survival, respiratory function or cardiovascular health, although it showed improved school or work attendance rates [71]. When oxygen is administered during exercise only, it helps to improve oxygenation, reduces the feeling of dyspnoea and increases the duration of the exercise [71, 72]. However, supplemental oxygen during exercise in patients with initially low arterial oxygen values appears to cause hypercapnia in the short term (PCO_2 up to 16 mmHg) [71]. Also, oxygen therapy during sleep improves oxygenation, but is accompanied by small hypercapnia [71]. The use of supplemental oxygen should follow the established clinical guidelines that are based on hypoxia ($PaO_2 \leq 55$ mmHg or 60 mmHg) and the presence of clinical symptoms [73].

Non-invasive ventilation (NIV) is used in patients with CF on respiratory failure, hypoventilation during sleep, as well as a bridge to lung transplantation [3]. For patients with severe clinical presentation where airway clearance causes fatigue and high levels of dyspnoea, NIV can be used to assist airway clearance [74]. The use of NIV during the physiotherapy session facilitates mucus expectoration and reduces the sensation of dyspnoea during the treatment compared to other

techniques particularly for patients with low lung function [75]. However, the long-term effects of NIV on airway clearance need further investigation [76].

Paediatric population

Choosing a treatment plan for children with CF is based on age, clinical presentation and certain social criteria [77]. There is no agreement on the most appropriate starting age for airway clearance. A proposal for early disease management (pre-symptomatic) is to carefully monitor the clinical presentation of children and adopt an active treatment plan following the onset of symptoms [78]. At young ages, where the child can not follow instructions and cooperate, assisted autogenic drainage or PEP devices with a child mask can be used. Physiotherapists are also responsible for educating the child's parents or carers for appropriate evaluation of the child's symptoms and treatment implementation as required [79]. Postural drainage with tilt (head-down positions) is no longer advised for babies, as it has been shown to increase the gastroesophageal reflux [80].

As children grow older, they can more actively participate in their treatment. Children over 3 years old can also use an airway clearance game, the bubble PEP. This is a positive-pressure breathing home-made device, where children are encouraged to generate soap bubbles by breathing out through a small plastic tube and into a bottle of soapy water [81]. According to the UK Cystic Fibrosis Foundation, at the age of 6 years or more, the use of nebulised hypertonic saline can be initiated in combination with airway clearance [82]. Also, at all ages, activity games and engagement with exercise are encouraged and used, for instance racing, trampolines and exercises using a gym ball [83].

Palliative care

CF is a disease that limits life expectancy and requires discipline and consistency to many hours of daily treatment. As a result, its psychological impact should not be ignored [84]. If patients are in respiratory failure and in lung transplantation list, pulmonary rehabilitation is the treatment priority, alongside the aim to relieve symptoms. Working in line with the patient's wishes is very important, particularly during the palliative care stage. Airway clearance of less active patient participation (eg. postural drainage), massage and some dyspnoea relieving positions could be applied during this stage, if they provide comfort to the patient [85].

CONCLUSIONS

CF management is highly demanding, mainly aiming to the reduction and treatment of chest infections, improvement of quality of life and increase of life expectancy. Physiotherapy is an integral part of the patient's daily treatment routine, and additionally to airway clearance other important issues should be addressed. International clinical guidelines suggest access to specialised physiotherapy care both during a clinically stable stage of the disease and during respiratory infections. At the clinically stable stage, patients should be evaluated by physiotherapists every 3-6 months to re-evaluate and optimize their treatment plan. During respiratory infections, physiotherapy interventions are intensified according to the clinical presentation. Although in CF airway clearance is the cornerstone of physiotherapy treatment, physiotherapists work beyond the respiratory system and play an important role in the management of other issues, mainly using individualised exercise programmes. The exercise programmes need to be tailored to patient-related needs and issues, such as pain, diabetes and incontinence. This way, the patient-centred and individualised treatment follows the international standards and clinical guidelines.

Table 1. Common airway clearance techniques and methods.

Airway clearance techniques
Postural drainage
Manual techniques
Active circle of breathing techniques (ACBT)
Autogenous drainage (AD)
Positive expiratory pressure (PEP) devices (PEP mask, Pari-PEP, etc)
Positive expiratory pressure (PEP) devices with oscillation (flutter, acapella, cornet, etc.)
Intermittent Positive Pressure Breathing (IPPB)
High frequency chest wall oscillation (HFCWO) or vest
Non-invasive mechanical ventilation (NIV)
Aerobic exercise

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